REMARKS

Claims 1-9, 11-15, 18-20, 23, 24, 27, 28 and 41-52 have been canceled. New Claims 57-61 have been added. Claims 53-61 are pending.

The Abstract has been amended to consist of a single paragraph of less than 150 words.

Support for Claims 57 and 58 is found, for example, at page 3, lines 19-34.

Support for Claims 59-61 is found, for example, at page 30, lines 1-17.

Further remarks appear below under appropriate subheadings.

Paragraph 2. Request for Reconsideration of Withdrawal of Claim 53 and Request for Rejoinder of Claims 54-56 and 59-61

Claims 46-56 were withdrawn from consideration by the Examiner for the same reasons that non-elected method Claims 41-45 were withdrawn. (Office Action at page 2.)

It appears that Claim 53 was withdrawn in error, because Claim 53 is drawn to a humanized immunoglobulin or antigen-binding fragment thereof. Applicants request that Claim 53 and new Claims 57 and 58 be examined on the merits, and that Claims 54-56, drawn to methods, and Claims 59-61, drawn to a composition, be rejoined if Claim 53 is found to be allowable.

Paragraph 4. Objection to Abstract

The Abstract has been amended to consist of a single paragraph of fewer than 150 words.

Rejection Under 35 U.S.C. § 102

Paragraph 7. Rejection of Claims 1, 2, 4-9, 13, 18, 23, 27 and 28 Under 35 U.S.C. § 102(e) as being anticipated by Ringler *et al.* (U.S. Patent No. 6,551,593).

Claims 1, 2, 4-9, 13, 18, 23, 27 and 28 have been canceled, obviating the rejection.

Claim 53 is not anticipated by Ringler *et al.* Claim 53 recites that the humanized immunoglobulin or antigen-binding fragment comprises a heavy chain that comprises the variable region of SEQ ID NO:19 and a light chain that comprises the variable region of SEQ ID NO:21. The recited variable region sequences are not the same as the variable region sequences

of the murine Act-1 antibody. (Compare SEQ ID NO:15 (murine Act-1 V_H with composite signal peptide) with SEQ ID NO:19; and SEQ ID NO:12 (murine Act-1 V_L with signal peptide) with SEQ ID NO:21.) Accordingly, the sequences recited in Claim 53 are not inherent in the murine Act-1 antibody.

Rejections Under 35 U.S.C. § 103

Paragraph 9. Rejection of Claims 1-9, 11-15, 18-20, 23, 24, 27 and 28 Under 35 U.S.C. § 103(a) as being obvious over Queen *et al.* (U.S. Patent No. 5,530,101) in view of Lazarovits *et al. (J. Immunol. 151*:6482-6489 (1993)) and further in view of Ringler *et al.* (U.S. Patent No. 6,551,593) and the art known 21/28'CL and GM6076'CL antibody sequences.

Paragraph 10. Rejection of Claims 1-9, 11-15, 18-20, 23, 24, 27 and 28 Under 35 U.S.C. § 103(a) as being obvious over Queen *et al.* (U.S. Patent No. 5,530,101) in view of Lazarovits *et al. (J. Immunol. 151*:6482-6489 (1993)) and further in view of the art known 21/28'CL and GM6076'CL antibody sequences, as evidenced by Tiisala *et al.* or Mawhorter *et al.* or Yuan *et al.* or Schulz *et al.* or Nieto *et al.*

Pareagraph 11. Rejection of Claims 1-9, 11-15, 18-20, 23, 24, 27 and 28 Under 35 U.S.C. § 103(a) as being obvious over Queen *et al.* (U.S. Patent No. 5,530,101) in view of Lazarovits *et al. (J. Immunol. 151*:6482-6489 (1993)), Springer *et al.* (Leukocyte Typing V), Petell *et al.*, Huston *et al.* (U.S. Patent No. 5,258,498) and further in view of the art known 21/28'CL and GM6076'CL antibody sequences.

Claims 1-9, 11-15, 18-20, 23, 24, 27 and 28 have been cancelled, obviating the rejections under 35 U.S.C. § 103.

Claim 53 is not obvious over any of the cited combinations of references. Claim 53 recites that the humanized immunoglobulin or antigen-binding fragment comprises a heavy chain that comprises the variable region of SEQ ID NO:19 and a light chain that comprises the variable

region of SEQ ID NO:21. The recited variable region sequences are not inherent in the murine Act-1 antibody.

When novel compounds are claimed using structural terms, a *prima facie* case of obviousness requires that the prior art suggest the claimed compounds themselves to the person of ordinary skill in the art. In re Deuel, 34 USPQ2d 1210, 1214 (Fed. Cir. 1995). A particular result is not made obvious by a general incentive or the existence of techniques suitable to achieve the result. Id., at 1216. Accordingly, the subject matter of Claim 53 is not obvious.

In addition, the specification contains objective evidence showing that the subject matter of Claim 53 is not obvious. The Examiner's attention is directed to page 105, lines 9-27 which describe the results of cross competition studies using murine Act-1 antibody and LDP-02. LDP-02 is a humanized antibody comprising a heavy chain having the variable region of SEQ I D NO:19 and a light chain having the variable region of SEQ ID NO:21. (See, *e.g.*, the Brief Descriptions of Figures 11 and 12 at pages 7-8 regarding the variable region amino acid sequences of LDP-02.) The specification teaches that the results of the cross competition studies demonstrated that "LDP-02 was specific for the epitope recognized by murine Act-1, and that its binding affinity was better than that of the murine antibody." (Specification at page 105, lines 25-27.)

These results are surprising because the person of skill in the art at the time the application was filed would have hoped that the humanized antibody had an affinity that was, at best, about 90% of the affinity of the original nonhuman antibody. Evidence is provided by Queen *et al.* (U.S. Patent No. 5,530,101). Queen *et al.* teach that "a major problem with present humanization procedures has been a loss of affinity for the antigen, in some instances as much as 10-fold or more, especially when the antigen is a protein." (Queen *et al.* at column 2, lines 9-13. (Citations omitted).) Queen *et al.* further teach that their method can produce humanized antibodies that "[i]deally, ... will exhibit affinity levels at least about 60 to 90% of the donor immunoglobulin's original affinity to the antigen." (Id. at column 3, lines 39-42.)

In view of the art-recognized problem of loss of affinity for antigens associated with humanization, and the teachings of Queen *et al.* that ideally a humanized antibody retains at least about 60% to 90% of the affinity of the donor antibody. The higher affinity of LDP-02 as compared with the Act-1 antibody is surprising.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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